REMARKS

Following entry of the foregoing amendments, claims 1, 7 to 9, 11, 13 to 24, 26, 27, 36, 38 to 52, 59, 62, and 68 will be pending in the application. Claim 1 has been amended, and claims 2 to 6, 10, 12, 25, 28 to 35, 37, 53 to 58, 60, 61, and 63 to 67 have been canceled, herein, without prejudice. New claim 68 has been added. Support for the amendments is found throughout the specification as originally filed, and the amendments thus do not introduce new matter into the application. Claims 11, 13 to 24, 26, 27, 36, and 38 to 52 have been withdrawn from consideration as drawn to non-elected subject matter.

Applicants respectfully request reconsideration of the rejections of record in view of the foregoing amendments and the following remarks.

Priority

The Office asserts that the applications to which the present application claims priority, except provisional application number 60/423,760, do not provide adequate support for subject matter recited in the claims. Specifically, the Office asserts that support does not exist in the priority applications for compositions comprising two chemically synthesized oligomers that are at least partially complementary.[1] The subject matter of the present claims is, however, adequately supported by the specification of U.S. application number 08/870,608, filed June 6, 1997 ("the 608 application"), and the claims are thus entitled to the benefit of the filing date of the 608 application.

Preliminarily, applicants note that claim 1 has been amended, and claims 2 to 6, 12, 25, 28 to 35, 37, 53 to 58, 60, 61, and 63 to 67 have been canceled, herein. Exemplary support in the 608 application as originally filed for each of the pending claims as amended herein is indicated in the table below.

[1] Office action dated October 2, 2006, page 3.

Claim	Exemplary support in the specification of the 608 application
1	Page 92, line 10 to page 93, line 27; page 7, lines 13 to 16; page 7, lines 28 to 31; and page 6, line 34 to page 7, line 2
7	Page 92, line 10 to page 93, line 27
8	Page 92, line 10 to page 93, line 27
9	Page 7, lines 28 to 37
10	Page 6, line 34 to page 7, line 2
59	Page 27, lines 24 to 29
68	Page 92, line 10 to page 93, line 27

As indicated in the table above, the subject matter of the pending claims is fully supported by the 608 application as originally filed. For example, page 92, line 10 to page 93, line 27 of the specification of the 608 application (Example 27) describes exemplary chemically synthesized oligomer duplexes comprised of a "sense" oligonucleotide strand and an "antisense" oligonucleotide strand. The two strands of the oligomer duplexes are not covalently linked.

Page 7, lines 13 to 16 of the specification of the 608 application indicate that the oligomers described in the specification are preferably 12 to 30 nucleoside subunits in length. Notably, these portions of the specification are not limited to describing the length of single-stranded oligomers. Accordingly, those skilled in the art would understand that any of the oligomers described in the specification, whether single-stranded or part of a duplex, are preferably 12 to 30 nucleoside subunits in length.

In addition, page 7, lines 28 to 31 of the specification of the 608 application indicate that the oligomers described in the specification are specifically hybridizable to a preselected RNA target.

Page 7, lines 28 to 36 of the specification of the 608 application also indicate that the chimeric oligomeric compounds comprise a segment having a plurality of ribofuranosyl nucleoside subunits. Again, this description is not limited to single-stranded oligomers, and

those skilled in the art would thus understand that any of the oligomers described in the specification, including oligomer duplexes, could contain such nucleoside subunits.

The 608 application describes oligomers that contain ribonucleosides modified to improve at least one of the oligomer's pharmacokinetic properties (page 6, line 34 to page 7, line 2). As understood by those skilled in the art, the "pharmacokinetic properties" of an oligomer include the oligomer's degree of nuclease resistance and the thermal stability of a duplex formed by the oligomer and a complementary oligomer. At the time the 608 application was filed, it was known in the art that 4'-thio ribonucleosides impart increased resistance to calf spleen phosphodiesterase, snake venom phosphodiesterase, endonuclease S1, and ribonuclease A to an oligomer containing the 4'-thio ribonucleosides relative to the corresponding oligomer containing ribonucleosides (Bellon, L., *et al.*, *Nucleic Acids Res.*, 1993, 21(7), 1587-1593, at 1591, attached as Exhibit A). It was also known in the art at the time the 608 application was filed that 2'-deoxy-4'-thio ribonucleosides impart increased resistance to endonuclease S1 to an oligomer containing the 2'-deoxy-4'-thio ribonucleosides relative to the corresponding oligomer containing 2'-deoxy nucleosides (Jones, G.D., *et al.*, *Nucleic Acids Res.*, 1996, 24(21), 4117-4122, at 4120-4121, attached as Exhibit B).

Moreover, it was also known in the art at the time the 608 application was filed that introduction of 4'-thio ribonucleosides into an oligomer improves the thermal stability of a duplex formed between the modified oligoribonucleotide and a complementary unmodified oligoribonucleotide (Exhibit A at 1592). Similarly, it was also known in the art at the time the 608 application was filed that introduction of 2'-deoxy-4'-thio ribonucleosides into an oligomer improves the thermal stability of a duplex formed between the modified deoxyoligoribonucleotide and a complementary unmodified deoxyoligoribonucleotide (Exhibit B at 4119). The 608 application thus describes oligomers containing ribonucleosides modified to improve their nuclease resistance and thermal stability, which those skilled in the art would have understand at the time the 608 application was filed to have included oligomers containing 4'-thio ribonucleosides and 2'-deoxy-4'-thioribonucleosides.

Finally, page 27, lines 24 to 29 of the specification of the 608 application describe compositions comprising the oligomers described throughout the specification and a pharmaceutically acceptable carrier.

Support for each element of the amended claims thus exists in the specification of the 608 application as originally filed. The present application is therefore entitled to the benefit of the filing date of the 608 application, which is June 6, 1997.

Alleged Double Patenting

Claims 1 to 10, 12, 25, 28 to 35, 37, and 53 to 58 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claim 24 of copending U.S. patent application number 10/700,697. Applicants request deferral of this rejection pending the identification of some allowable subject matter in the present application, as the rejection likely can be readily resolved, depending upon the subject matter ultimately allowed, through the filing of a suitable terminal disclaimer.

Claim Objections

Claims 12 and 37 have been objected to as allegedly containing non-elected subject matter, and claims 12, 25, and 37 have been objected to for allegedly failing to further limit the subject matter of a claim from which they depend. Without conceding the correctness of the objections, claims 12, 25, and 37 have been canceled. Applicants accordingly, respectfully request withdrawal of the objections.

Alleged Lack of Written Description

Claims 28 to 35, 37, and 62 to 64 have been rejected under 35 U.S.C. § 112, first paragraph for allegedly failing to comply with the written description requirement. Without conceding the correctness of the rejection, and to advance prosecution, claims 28 to 35, 37, and 62 to 64 have been canceled. Applicants accordingly, respectfully request withdrawal of the rejection.

Alleged Lack of Enablement

Claims 59 to 67 have been rejected under 35 U.S.C. § 112, first paragraph for allegedly failing to comply with the enablement requirement. Without conceding the correctness of the rejection, and to advance prosecution, claims 60, 61, and 63 to 67 have been canceled, obviating the rejection with respect to those claims.

Claim 59 has been rejected because the claim recites a "pharmaceutical composition," but the specification allegedly fails to enable the use of the claimed composition as a therapeutic agent. Without conceding the correctness of the assertion, and to advance prosecution, claim 59 has been amended to delete the word "pharmaceutical" from the preamble of the claim, obviating the rejection.[2] Applicants accordingly, respectfully request withdrawal thereof.

With respect to claim 62, the Office concedes that the specification is enabling for methods of decreasing the expression of a target gene in a cell *in vitro*, but asserts that the specification does not enable methods of modulating expression of a target gene in an animal *in vivo*.[3] Without conceding the correctness of the assertion, and to advance prosecution, claim 62 has been amended to recite methods of decreasing the expression of a target nucleic acid in a cell *in vitro* comprising contacting the cell with a composition of claim 1. The rejection has thus been obviated, and Applicants respectfully request withdrawal thereof.

Alleged Obviousness

A. Claims 1 to 10, 12, 25, 53 to 59, 61, 62, and 64 have been rejected under 35 U.S.C. § 103(a) as allegedly obvious over published PCT application number WO 94/01550 ("the Agrawal application") in view of U.S. patent number U.S. 5,639,873 ("the Barascut patent"). Applicants respectfully request reconsideration and withdrawal of the rejection because the Agrawal application and the Barascut patent, when considered individually or in combination, fail to teach or suggest every limitation of the present claims.

[2] "The rejection with regard to claims 59-61 may be overcome by removing the word 'pharmaceutical' from the preamble of these claims." Office action dated October 2, 2006, page 10.
[3] Office action dated October 2, 2006, page 9.

To establish *prima facie* obviousness, the Patent Office must demonstrate that the cited prior art reference or combination of references teaches or suggests ***all*** the limitations of the claims. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974); *In re Wilson*, 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970).

Applicants note that claim 1 has been amended to recite compositions comprising first and second oligomers that are not covalently linked, wherein at least a portion of the first oligomer is capable of hybridizing with at least a portion of the second oligomer, and each of the oligomers includes at least one 4'-thioribonucleoside or 2'-deoxy-4'-thioribonucleoside. The Agrawal application and the Barascut patent, when considered individually or in combination, fail to teach or suggest such compositions.

For example, the Agrawal application describes self-stabilized oligonucleotides having a target hybridizing region and a self-complementary region.[4] The application explains that the self-complementary region can be connected to the target hybridizing region by a suitable non-nucleic acid linker.[5] Examples of such linkers are said to include alkyl groups and an (ethylene glycol)$_{1-6}$ linker.[6] The application fails to teach or suggest, however, compositions comprising first and second oligomers *that are not covalently linked*, wherein at least a portion of the first oligomer is capable of hybridizing with at least a portion of the second oligomer, and each of the oligomers includes at least one 4'-thioribonucleoside or 2'-deoxy-4'-thioribonucleoside.

The Barascut patent also fails to teach or suggest such compositions. The patent describes oligonucleotides comprising 4'-thiorobonucleotides or 4'-thio-2'-deoxyribonucleotides,[7] but fails to describe or suggest compositions comprising *first and second oligomers that each include at least one 4'-thioribonucleoside or 2'-deoxy-4'-thioribonucleoside* and that are not covalently linked, wherein at least a portion of the first oligomer is capable of hybridizing with at least a portion of the second oligomer.

[4] Page 5, lines 13 to 17.
[5] Page 15, lines 31 to 33.
[6] Page 15, lines 33 to 36.
[7] Col. 2, lines 14 to 19.

Since the Agrawal application and the Barascut patent, when considered individually or in combination, fail to teach or suggest every limitation recited in the present claims, the references fail to render the claimed subject matter obvious. Applicants accordingly, respectfully request withdrawal of the rejection.

B. Claims 1 to 10, 12, 25, 28 to 35, 37, and 53 to 64 have been rejected under 35 U.S.C. § 103(a) as allegedly obvious over published U.S. patent application number U.S. 2004/0029275 ("the Brown application") in view of the Barascut patent. Applicants respectfully request reconsideration and withdrawal of the rejection because the Brown application is not available as prior art against the present application due to the fact that the present application is entitled to the benefit of the filing date of U.S. patent application number 08/870,608, filed June 6, 1997 ("the 608 application").

As discussed above in connection with the claim of priority made for the present application, support for each element of the pending claims exists in the specification of the 608 application as originally filed. The present application is thus entitled to the benefit of the filing date of the 608 application, which is June 6, 1997. Since this date is before the priority date of the Brown application, the Brown application is not available as prior art against the present application. The rejection for alleged obviousness based on this reference is thus improper, and Applicants accordingly, respectfully request withdrawal thereof.

Conclusion

Applicants believe that the foregoing constitutes a complete and full response to the official action of record. Accordingly, an early and favorable action is respectfully requested.

Respectfully submitted,

Date: December 19, 2006

/Jane E. Inglese/
Jane E. Inglese, Ph.D.
Registration No. 48,444

Woodcock Washburn LLP
Cira Centre, 12th Floor
2929 Arch Street
Philadelphia PA 19104
Telephone: (215) 568-3100
Facsimile: (215) 568-3439